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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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GATES & COOPER LLP
HOWARD HUGHES CENTER
6701 CENTER DRIVE WEST, SUITE 1050
LOS ANGELES, CA 90045

EXAMINER
CHEN, LIPING

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/04/2002

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/730,716	Applicant(s) SUNG ET AL.	
	Examin r Liping Chen	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/28/2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-11,13 and 15-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-11,13 and 15-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 December 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

Applicant's election with traverse of group V, claim 13, in Paper No. 7, is acknowledged. The traversal is on the ground(s) that the Examiner has not shown that a serious burden would be required to examine all the claims. In particular, Applicants submit that the vaccine of claim 13 is novel and nonobvious should provide the necessary information for examination of the remaining claims without requiring an additional search effort. This is found persuasive. Therefore, the restriction is withdrawn. Claims 4, 12 and 14 are cancelled. Claims 1-3, 6-11 and 13 are amended. The new claims 15-22 have been entered.

Claims 1-3, 5-11, 13 and 15-22 are pending and are under current consideration.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Korea on 12/06/1999. It is noted, however, that applicant has not filed a certified English Translation copy of the Korea application as required by 35 U.S.C. 119(b).

Specification

The disclosure is objected to because of the following informalities:

The abstract of the disclosure is objected to because it comprises three paragraphs. An abstract should contain only a single paragraph on a separate sheet within the range of 50 to 150 words. Correction is required. See MPEP § 608.01(b).

The specification, page 22, line 6, states (Group 1), it is not consistent with the results in figures provided. It is suggested this be written as (Group 2).

The specification, page 22, line 9, states (Group 2), it is not consistent with the results in figures provided. It is suggested this be written as (Group 1).

Fig. 9 is objected to because the plasmid names used in the figure are not consistent with the names used in the specification or other figures, such as it is not clear if pTV-GE in the figure is equivalent to pTV-SIV/GE in the specification and other figures. Applicant is advised that the same name should be used for the same plasmid through the specification.

Claim Rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-3, 10-11, 15-16 and 21-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 10, 15 and 21, as written are indefinite because they refer to Fig. 1. Claims must stand alone to define invention. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." *Ex parte fressola*, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations ommitted).

Claims 3, 11, 16 and 22, as written are indefinite because they refer to Fig. 2. Claims must stand alone to define invention. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." *Ex parte fressola*, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations ommitted).

Claims 3 and 16, as written are indefinite because they refer to accession NO:KCTC 0702BP. It is not clear if the limitation is only for pTV-SIV/GE plasmid or the limitation includes the deposited cell (DH5α cell) containing the plasmid.

Claims 7 and 18 are indefinite as written. The claims are directed to the site responsible for enzyme activity of integrase is at portions of 5130-5135, and wherein the bases at positions 5130-5132 are deleted, and the bases at positions 5133-5135 are substituted by a codon for serine. The claims are indefinite because there is no uniform numbering system provided. Therefore, for example, it is not known what positions 5130-5135 correspond to.

Claim 13, as written is indefinite because it refer to "... and/or...". It is not clear which is the claimed scope.

Claims 11 and 22, as written are indefinite because they refer to accession NO:KCTC 0703BP. It is not clear if the limitation is only for pTV-SIV/GE plasmid or the limitation includes the deposited cell (DH5α cell) containing the plasmid.

Claim Rejections - 35 USC § 112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13, 15-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling a vaccine comprising pTV-SIV/GE+pTV-SIV/pol that prevents SIV infection in rhesus monkeys, does not reasonably provide enablement for all other vaccines. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 13 is directed to a DNA vaccine for prevention and/or treatment of AIDS comprising: a first plasmid carrying gag, dpol, env and rev gene, wherein the gag, dpol, env and rev gene are derived from SIV, and wherein the first plasmid lacks tat and nef genes; and/or a second plasmid carrying a SIV-derived pol gene encoding for a reverse transcriptase and an integrase; Claims 15-22 are further directed to different embodiments: claims 15 and 16 are further directed to the first plasmid of claim 13 comprise SIV/GE gene (claim 15) or is pTV-SIV-GE (claim 16); claims 17 and 18 are directed the second plasmid of claim 13 encodes an inactive integrase; claims 19 and 20 are directed to the vaccine of claim 13, wherein 5'-end of pol gene of the second plasmid is linked to the signal sequence of a secretion protein; claims 20 and 21 are directed to the second plasmid of claim 13 comprises SIV/pol gene (claim 20) or is pTV-SIV/pol (claim 21).

The specification provides evidence that using 400 μg of each pTV-SIV/GE and pTV-SIV/pol by intramuscular injection into rhesus monkeys (see specification, page 22, line 1-8) 45 weeks before SIVmac239 challenge (see specification, page 23,

line 14-22) can prevent SIVmac239 infection as determined by monitoring for the parameters such as the virus load in the peripheral blood mononuclear cells (PBMC) (see specification, page 24, line 15 to page 25, line 27, and Fig. 4) and post challenge level of the p27 antigenemia (specification, page 28, line 25 to page 29, line 13, and Fig. 7). There is no evidence that use of any single plasmid such as pTV-SIV/GE or pTV-SIV/pol in any dosage or any mutated forms (pertaining to instant claims 17 and 18) or secretion forms (pertaining to instant claims 19 and 20) can result in the same prevention effect. In contrast to the broad claims, the working examples presented by the instant specification show that immunization with plasmids containing different genes in pTV-SIV/GE and pTV-SIV/pol as indicated in the result of group 3, which uses 200 μg of each pTV-SIV/GE and pTV-SIV/pol, and 200 μg of each pTV-SIV/GE-CG, a pTV-SIV/GE containing human GM-CSF gene (specification, page 20, line 25 to page 21, line 6), and pTV-SIV/pol-IL2, a pTV-SIV/pol containing IL-2 gene (specification, page 20, line 16-20), failed to prevent SIV infection in rhesus monkeys. Similarly, adding boosting immunization after the initial immunization with 400 μg of each pTV-SIV/GE and pTV-SIV/pol (group 4) result failed to prevent SIV infection in rhesus monkeys. The working examples provided by the specification do not appear to suggest that any DNA vaccine claimed can prevent SIV infection in rhesus monkeys. Moreover, the evidence of record fails to demonstrate that any combination of plasmids can treat rhesus monkeys or humans that have AIDS. The difficulty in vaccine development

in AIDS prevention and treatment has been well recognized due to non-cross reacting between different strains and lack of animal models. Daniel et al. (Science 258:1938-1941, 1992) states that the difficulty in AIDS vaccine development is the persistent, unrelenting nature of HIV and SIV infection once infection is initiated (Daniel, Abstract) and the large number of HIV-1 strains that are non-or minimally cross-neutralizing (Daniel, page 1938, first parag.). The difficulty in achieving protection against HIV and SIV has been borne out to varying degrees by vaccine trials in animal models including the limited success in chimpanzee trials (Daniel, page 1938, middle col. sec. parag. to the end). This difficulty can also be observed from the working examples presented by the instant specification as suggested by the results of group 3 and group 4. The specification states that rhesus monkey models infected by SIVmac virus are recognized as being the closest model to HIV-infected humans (specification, page 3, line 18-20). However, Hanke et al. (J. Virol. 73:7524-7532, 1999) state that for HIV infection and AIDS, infection of nonhuman primates with immunodeficiency viruses offers a spectrum of models in terms of disease severity and difficulty in preventing virus infection. These models range from the infection of chimpanzees with HIV-1 SF2, a model in which neutralizing antibodies provide protection, to infection of rhesus macaques with simian immunodeficiency virus SIVmac, in which a role for cell-mediated immune responses in partial or complete protection is strongly supported. In turn, only results from clinical trials will show which of these monkey models is the closest to

HIV infection of humans (Hanke, page 7524, right col.). Further, Smith et al. (Viral Immunol 13:343-351, 2000) state that it has become increasingly clear that the use of classic vaccine approaches are not sufficient to develop a successful vaccine against human immunodeficiency virus (HIV) or its simian counterpart, simian immunodeficiency virus (SIV). Subunit vaccines comprising killed or inactivated virus, recombinant vaccinia virus expressing SIV proteins, and synthetic peptides representing immunogenic regions of the envelope protein are some of the vaccine candidates that have been tested in the SIV-rhesus macaque model system. These vaccines have demonstrated that complete protection from infection and progression to disease is extremely hard to achieve against SIV. An effective vaccine will likely elicit both a humoral and cellular immune response, but a clear understanding of the specific immunological correlates of protection in these studies still awaits further investigation (Smith, page 343, last parag.). In the instant invention, incomplete cell-mediated immune response can be observed in group 2, number 8780 (Fig. 4), which also shows an incompletely against SIV grown in rhesus monkey lymphocytes (Fig. 8).

Therefore, in view of the results obtained from the working examples, the quantity of experimentation necessary to determine the composition that are necessary for a DNA vaccine for SIV prevention, the lack of evidence and direction for development of any DVA vaccine for preventing other animal from AIDS, lack of evidence that any vaccine claimed can treat any AIDS, based upon the nature of the

invention, the state of the prior art, the non- or minimally cross-neutralizing between HIV-1 strains, no cross-reaction between HIV and SIV, lack of evidence that to use any different plasmid other than the combination pTV-SIV/GE and pTV-SIV/pol each of 400 μg will result in the prevention of rhesus monkey from SIV infection, the claimed invention would have required one skilled in the art to engage in an undue amount of experimentation without a predictable degree of success to achieve any specific and the breath of the invention.

Claims 3, 11, 16 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to two plasmids designated pTV-SIV/GE and pTV-SIV/pol. Since the plasmids are essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the plasmids are not so obtainable or available, the requirements of 35 U.S.C. 112, regarding "how to make", may be satisfied by a deposit of plasmids.

In the instant case, although, the specification states both plasmids have been deposited in Korean Collection for Type Culture of Korea Research Institute of Bioscience and Biotechnology (KRIBB) on Nov. 27, 1999 (specification, page 13, line

15-20). No address for the Korean repository has been provided. Further, there is no indication that the deposit was made under the terms of the Budapest Treaty. If the deposits are made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific plasmids have been deposited under the Budapest Treaty and that the vectors will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

(a) during the pendency of this application, access to the invention will afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request of for the effective life of the patent whichever is longer; and,

(d) a test of viability of the biological material at the time of deposit (see 37 CFR 1.807);

and,

(e) the deposit will be replaced if it should ever become inviable.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 5 and 13 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Smith et al. (Viral Immunol 13:343-51, 2000).

Claim 5 is directed to a plasmid carrying a SIV-derived pol gene encoding for a reverse transcriptase and an integrase. Claim 13 is directed to a DNA vaccine for prevention and/or treatment of AIDS comprising a plasmid carrying a SIV-derived pol gene encoding for a reverse transcriptase and an integrase.

Claim 13 recites the intended use of a DNA vaccine for prevention and/or treatment of AIDS. It is noted that an intended use of a product is not afforded patentable weight in a product claim where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand alone. The MPEP states that,".. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto , 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02).

Smith et al. teach a plasmid, pIV, containing pol/vpr gene fusion fragment from SIV for a DNA vaccine (Smith, Abstract, page 344, last parag., and Fig. 1), wherein the pol gene encodes reverse transcriptase, integrase and protease. Thus, Smith et al. clearly anticipates the claimed invention.

Claims 5 and 6 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Göttlinger et al. (U.S. Patent No. 6,479,281 B1, issued 11/12/2002).

Claim 5 is directed to a plasmid carrying a SIV-derived pol gene encoding for a reverse treascriptase and an integrase, claim 6 is further directed the plasmid of claim 5, wherein the integrase has been inactivated by modifying a site responsible for enzyme activity of integrase.

Göttlinger et al. ('281) teach to use any lentivirus, which belongs to retrovirus family, including primate lentiviruses such as HIV and SIV ('281. col. 10, line 65-66) for pol vector construction and claim a pol vector constructed from SIV ('281, col. 27, 28-30 and col. 28, line 44-47) with inactivated integrase ('281, col. 5, line 47, and col. 22, line 117-20). Since vector construction would require plasmid construction and amplification, Göttlinger et al. clearly anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naldini et al. (U.S. Patent No. 5,994,136, issued 11/30/1999) taken with Weiner et al. (U.S. Patent 5,981,505, issued 11/09/1999) and Daniel et al. (Science 258:1938-1941, 1992).

Claim 1 is directed to a plasmid carrying gag, protease, env and rev genes, wherein the gag, protease, env and rev genes are derived from SIV, and wherein the plasmid lacks tat and nef genes, claim 13 is directed to a DNA vaccine for prevention and/or treatment of AIDS comprising the plasmid described in claim 1.

Claim 13 recite the intended use of a DNA vaccine for prevention and/or treatment of AIDS. It is noted that an intended use of a product is not afforded patentable weight in a product claim where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand alone. The MPEP states that,".. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto , 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02).

Naldini et al. ('136) teach plasmid-based or virus-based ('136, col. 3, line 10-20) recombinant vectors using genes derived from HIV-1, HIV-2 and/or SIV ('136, col. 2, line 42-53). Naldini et al. ('136) teach that vectors lacking a functional tat gene are desirable for certain applications ('136, col. 3, line 1-2), where tat gene can be deleted in part or in whole ('136, col. 7, line 23-24). Naldini et al. ('136) further teach an improved version of the lentiviral vector in which the HIV virulence genes nef was deleted without compromising the ability of the vector to transduce non-dividing cells have been developed ('136, col. 8, line 39-42). However, Naldini et al. do not teach a plasmid-based vector or vaccine comprising SIV genes that lack of tat and nef.

Weiner et al. ('505) teach a plasmid derived from HIV with safety features including a tat deletion and a 50% deletion of nef and the use of CMV promoter and

a non-retroviral poly(A) site ('505, col. 39, line 35-37). Weiner et al. ('505) states that in contrast to tat and rev, which clearly play essential roles in HIV replication, other regulatory proteins such as nef, vpr, vif, and vpu are sometimes referred to as "accessory" proteins. Primate recombinant viruses deleted in either vpr, nef or vif are non-pathogenic *in vivo* ('505, col. 49, line 29-32 and line 42-44). Weiner et al. cure the deficiency of Naldini et al. in that it provides a teaching for developing plasmid from HIV with safety feature by deleting tat and 50% nef.

Further, Dianiel et al. (Science, 1992) teach Rhesus monkeys vaccinated with live SIV deleted in nef were completely protected against challenge by intravenous inoculation of live, pathogenic SIV. Dianiel et al. cure the deficiency of both Weiner et al. and Dianiel et al. in that it provides evidence that nef gene deletion improves the safety feature when using a live SIV virus for prevention and nef gene is not required for vaccination.

At the time the claimed invention was made, methods of producing a recombinant vector were within the routine skill of the ordinary artisan as evidenced by Naldini et al. ('136) and Weiner et al. ('505). Accordingly, in view of the teachings of Weiner et al ('505), it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was made, to modify the vector of Naldini et al. ('136) to construct a plasmid using genes derived from SIV with both tat and nef deletion to improve the safety feature with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to

make such a modification to develop plasmid-base vector as it was an art-recognized goal to develop a plasmid based vector with improved safety feature, particularly since Weiner et al. ('505) teach to delete nef gene to increase vector safety feature, and Dianiel et al. demonstrate that the safety feature of using live SIV with nef gene deletion as vaccine. At the time the claimed invention was made, methods of producing a recombinant vector were within the routine skill of the ordinary artisan as evidenced by Naldine et al. ('136) and Weiner et al. ('505).

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claims 5 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gŏttlinger et al. (U.S. Patent No. 6,479,281 B1, issued 11/12/2002) in view of Morris-Vasios et al. (J Virol 62:349-353, 1988).

Claim 5 is directed to a plasmid carrying a SIV-derived pol gene encoding for a reverse transcriptase and an integrase. Claim 8 is directed to the plasmid of claim 5, wherein the 5'-end of pol gene is fused to signal sequence of a secretion protein.

Gŏttlinger et al. ('281) teach to use any lentivirus, which belongs to retrovirus family, including primate lentiviruses such as HIV and SIV ('281. col. 10, line 65-66) for pol vector construction and claim a pol vector constructed from SIV ('281, col. 27, 28-30 and col. 28, line 44-47) with inactivated integrase ('281, col. 5, line 47, and col. 22, line 117-20). The vector taught by Gŏttlinger includes plasmid. However,

Göttlinger et al. ('281) does not teach to fuse 5'-end of pol gene to signal sequence of a secretion protein.

Morris-Vasios et al. teach to fuse the 5'-end the gene encoding avian sarcoma-leukosis retrovirus pol-endo protein to a secretory signal sequences of an interleukin-2 receptor gene (Morris-Vasios, page 349, Abstract and page 351, left col. line 2-3) to study the function of pol gene product (Morris-Vasios, page 349, left col. first parag.).

At the time the claimed invention was made, methods of producing a fusion proteins were within the routine skill of the ordinary artisan as evidenced by Morris-Vasios et al. Thus, one of skill in the art of vector development using SIV gene would be motivated to modify the teachings of Göttlinger et al to construct a vector with 5'-end of pol gene derived from SIV fused to a signal sequence of a secretion protein taught by Morris-Vasios et al. to study the function of pol gene product with a reasonable expectation of success. Therefore, at the time the invention was made it would have been prima facie obvious to modify the teaching of Morris-Vasios et al. by fusing 5'-end of pol gene to signal sequence of a secretion protein as taught by Morris-Vasios et al.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over over Gŏttlinger et al. (U.S. Patent No. 6,479,281 B1, issued 11/12/2002) in view of Morris-Vasios et al. (J Virol 62:349-353, 1988) as applied to claims 5 and 8 above, and further in view of Hazama et al. (Vaccine 11:629-36, 1993).

Claim 9 is directed to the plasmid of claim 8, wherein the secretion protein is glycoprotein D of herpes simplex virus.

The plasmid carrying a SIV-derived pol gene encoding for a reverse treascriptase and an integrase, wherein the 5'-end of pol gene is fused to signal sequence of a secretion protein is rendered obvious in view of Gŏttlinger et al. ('281) and Morris-Vasios et al for the reasons previously discussed. However, both Gŏttlinger et al. ('281) and Morris-Vasios et al do not teach to fuse 5'-end of pol gene to signal sequence of glycoprotein D of herpes simplex virus.

Hazama et al. teach to fuse IL-2 to a truncated herpes simplex virus type 1 glycoprotein D to increase IL-2 antiviral activity as glycoprotein D as been studies as a potential HSV vaccine (Hazama, page 629 to 630 left col.).

Thus, one of skill in the art of vaccine development using SIV gene would be motivated to combine the teachings of Gŏttlinger et al., Morris-Vasios et al. and Hazama et al to fuse 5'-end of pol gene from SIV to signal sequence of glycoprotein D of herpes simplex virus for pol gene product function study with an expectation of increasing vaccine immunity when using the vector for vaccine. Therefore, at the time the invention was made it would have been prima facie obvious to modify the

teaching of Morris-Vasios et al. and Morris-Vasios et al. by fusing 5'-end of pol gene to signal sequence of glycoprotein D of herpes simplex virus as taught by Hazama et al.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liping Chen, whose telephone number is (703) 305-4842. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time). Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to Dianiece Jacobs, Patent Analyst, at (703) 305-3550. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-8724.

Liping Chen, Ph.D.
Patent Examiner
Group 1632

Art Unit 1632